Structure of the Voltage-Dependent Potassium Channel Beta Subunit in Complex With the Cytoplasmic Tetramerization Domain

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Introduction: Voltage-dependent Potassium channels are an integral component of the electrical signal generating system in cells which underlies muscle contraction, hormone secretion, and information processing in the central nervous system. Our laboratory aims to understand the basis of potassium channel operation through structure determination by X-ray crystallography.

Results: The structure of the cytoplasmic assembly of voltage-dependent potassium channels was solved by X-ray crystallography at 2.1 angstrom resolution, by multiple isomorphous replacement, using synchrotron radiation at the X-25 Beamline. The assembly includes the cytoplasmic (T1) domain of the integral membrane α subunit together with the oxidoreductase β subunit in a four-fold symmetric $T1_4\beta_4$ complex. A complementary electrophysiological assay was used to demonstrate that this complex is oriented with four T1 domains facing the transmembrane pore and four β subunits facing the cytoplasm. The transmembrane pore communicates with the cytoplasm through lateral, negatively charged openings above the $T1_4\beta_4$ complex. The inactivation peptides of voltage-dependent potassium channels reach their site of action by entering these openings. In addition to bringing us one step close to visualizing the architecture of an entire voltage-dependent potassium channel, this structure implies a new mechanism acting in cell biology whereby cellular redox chemistry is coupled to membrane electrical activity.